P012 Intrarectal Administration Of Oxygenated Perfluorodecalin Promotes Healing Of Murine Colitis By Targeting Inflammatory Hypoxia.

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Objective: Intestinal inflammation is associated with enhanced mucosal hypoxia, which contributes to the ongoing inflammatory process and hampers appropriate mucosal healing. We questioned whether local treatment with an oxygen-carrying and -releasing molecule (oxygenated perfluorodecalin, O_2-PFD) could positively influence the course of experimental colitis.
Design: The impact of intrarectal treatment with O_2-PFD was tested using the murine dextran sodium sulfate (DSS)-induced model of distal colitis, both in preventive and therapeutic settings. Colonic mucosal hypoxia was visualized by pimonidazole-staining. Colonic permeability was evaluated with FITC-dextran.
Results: In the preventive study, mice treated with O_2-PFD were protected against DSS colitis compared to saline-treated mice, as demonstrated by reduced shortening of colon length, reduced colonic TNF-α levels and a lower histological inflammation score ($P<0.05$ for all parameters). In the therapeutic study, administration of O_2-PFD resulted in accelerated recovery of colitis compared to saline-treated littermates, and this was reflected by a better weight evolution, lower myeloperoxidase activity and a lower histological inflammation score ($P<0.05$ for all parameters).
It was found that O_2-PFD established its therapeutic effects through (i) intrinsic anti-inflammatory effects of the PFD molecule and (ii) O_2-induced preservation and healing of the intestinal epithelial surface. Further i*n vitro* and *in vivo* studies showed that the barrier-protective activity of O_2-PFD was obtained through prevention of colonocyte apoptosis and stimulation of colonocyte proliferation during inflammatory hypoxia.
Conclusions: These data show that intrarectal treatment with oxygenated PFD promotes colitis healing by the combined actions of direct anti-inflammatory effects and O_2-induced restitution of the epithelial barrier. As such, O_2-PFD enemas could be an attractive treatment option for patients with distal IBD.